PRVD2008-24

Proposed Re-evaluation Decision

# Maleic Hydrazide

*(publié aussi en français)*

**7 August 2008**

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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ISBN: 978-1-100-10361-7 (978-1-100-10362-4)
Catalogue number: H113-27/2008-24E (H113-27/2008-24E-PDF)

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# Overview

## What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the plant growth regulator maleic hydrazide, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing maleic hydrazide for sale and use in Canada.

An evaluation of available scientific information found that products containing maleic hydrazide do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of maleic hydrazide uses, new risk-reduction measures must be included on the labels of all products. Additional data are being requested as a result of this re-evaluation.

This proposal affects all end-use products containing maleic hydrazide registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for maleic hydrazide and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of maleic hydrazide.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

## What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

Maleic hydrazide, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration

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[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in the 1994 RED, the USEPA concluded that maleic hydrazide was eligible for reregistration provided risk-reduction measures were adopted. In addition, the USEPA published a Tolerance Reassessment Eligibility Decision (TRED) in 2005 for maleic hydrazide, which included an aggregate risk assessment. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in the RED and TRED were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation of this consultation document.

## What Is Maleic Hydrazide?

Maleic hydrazide is a plant growth regulator applied in the field to control sprouting of potatoes and onions while in storage or to grass and trees (e.g. along the edges of residential lawns in hard-to-mow areas, along highways, airport property, industrial areas, golf course roughs) to limit their growth. Maleic hydrazide is applied by air or by ground equipment, by farm workers and professional (custom) applicators.

## Health Considerations

### Can Approved Uses of Maleic Hydrazide Affect Human Health?

**Maleic hydrazide is unlikely to affect your health when used according to the revised label directions.**

Exposure to maleic hydrazide may occur through diet (food and water), working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that maleic hydrazide was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

### Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Maleic hydrazide is currently registered in Canada for use on potato and onion and could be used in other countries on crops that are imported into Canada. MRLs of maleic hydrazide are established for the following commodities: 50 ppm on potato, 15 ppm on onion and 30 ppm on beets, carrots and rutabagas. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set.

## Environmental Considerations

### What Happens When Maleic Hydrazide Is Introduced Into the Environment?

**Maleic hydrazide is unlikely to affect non-target organisms when used according to the revised label directions.**

Non-target organisms, including terrestrial plants, birds, mammals and non-vascular aquatic plants, could be exposed to maleic hydrazide in the environment. Environmental risk is assessed by the risk quotient method—the ratio of the estimated environmental concentration to the relevant effects endpoint of concern. The resulting risk quotients are compared to corresponding levels of concern. A risk quotient less than the level of concern is considered a negligible risk to non-target organisms, whereas a risk quotient greater than the level of concern indicates some degree of risk.

The USEPA concluded that the reregistration of maleic hydrazide was acceptable provided risk-reduction measures to further protect the environment were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required. Furthermore, the PMRA will require terrestrial buffer zones for maleic hydrazide to protect terrestrial plants from spray drift.

## Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of maleic hydrazide, the PMRA is proposing further risk-reduction measures for product labels.

**Human Health**

- Additional protective equipment to protect mixers/loaders/applicators
- A restricted-entry interval to protect workers entering treated sites

**Environment**

- Additional advisory label statements to reduce potential surface water and groundwater contamination
- Buffer zones to protect non-target, sensitive terrestrial habitats

## What Additional Scientific Information Is Required?

Data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. The registrants of this active ingredient must provide these data or an acceptable scientific rationale to the PMRA within the timeline specified in the decision letter. Appendix I lists all data requirements.

## Next Steps

Before making a final re-evaluation decision on maleic hydrazide, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

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2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

# Science Evaluation

## 1.0 Introduction

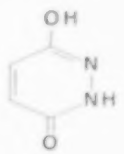
Maleic hydrazide is a plant grov. h regulator that acts by inhibiting cell division in plants.

Following the re-evaluation announcement for maleic hydrazide, the registrant of the technical grade active ingredient in Canada indicated its intention to provide continued support for all uses included on the labels of commercial end-use products in Canada.

The PMRA used recent assessments of maleic hydrazide from the United States Environmental Protection Agency (USEPA). The USEPA RED for maleic hydrazide, dated June 1994, and the USEPA TRED (USEPA 2005), as well as other information on the regulatory status of maleic hydrazide in the United States can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

## 2.0 The Technical Grade Active Ingredient, Its Properties and Uses

### 2.1 Identity of the Technical Grade Active Ingredient

| | |
|---|---|
| **Common name** | Maleic hydrazide |
| **Function** | Plant growth regulator |
| **Chemical family** | Pyridazine |
| **Chemical name** | |
| 1 **International Union of Pure and Applied Chemistry (IUPAC)** | 6-Hydroxy-2*H*-pyridazin-3-one |
| 2 **Chemical Abstracts Service (CAS)** | 1,2-dihydro-3,6-pyridazinedione |
| **CAS Registry Number** | 123-33-1 |
| **Molecular formula** | $C_4H_4N_2O_2$ |
| **Structural formula** |  |
| **Molecular weight** | 112.1 |

Identity of relevant impurities of human health or environmental concern:

- Hydrazine was found in both technical grades at levels of <1 to 2.3 ppm.

## 2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

| Property | Result |
|---|---|
| Vapour pressure | $3 \times 10^{-6}$ Pa (at 25°C) |
| Henry's law constant | **pH = Constant ($Pa \cdot m^3 \cdot mol^{-1}$)**<br>5 $5 \times 10^{-10}$<br>7 $3.5 \times 10^{-11}$<br>9 $3.2 \times 10^{-12}$ |
| UV–visible spectrum | Not expected to absorb UV at $\lambda > 300$ nm |
| Solubility in water at 25°C | pH 5: 590 mg/L<br>pH 7: 31 800 mg/L |
| *n*-Octanol–water partition coefficient | Log $K_{ow}$ = -0.99 (at pH 7) |
| Dissociation constant (p*K*a) | p*K*a = 3.4 |

## 2.3 Comparison of Use Patterns in Canada and the United States

Maleic hydrazide is a plant growth regulator/retardant (as a uracil antimetabolite) registered in Canada. It acts by inhibiting mitotic cell division in plants. It is applied in the field to potato and onion to control sprouting and resulting shrinkage during storage and to limit the growth of grass (rough turf areas and along the edges of residential lawns), trees or shrubs in order to reduce the need for mechanical mowing, pruning or shearing. It is applied to potato two to three weeks postbloom and two weeks before topkill or the first frost, and to onion 10 to 14 days prior to harvest. Maleic hydrazide is applied once per season with an application rate of up to 3.4 kg a.i./ha on potato and up to 2.25 kg a.i./ha on onion. The end-use products are formulated as soluble granules and applied as a spray to potato and onion by air or groundboom. Maleic hydrazide can also be applied as a spray to non-crop areas including grass (once per year in spring or fall), in hard-to-reach areas including hard-to-mow areas along highways/rights-of-way, airport property, edges of residential lawns, industrial areas, golf course roughs and similar areas by groundboom or hose-end sprayer. The end-use products can also be applied to trees and shrubs (once per season in the spring or early summer) by hose-end sprayer or airblast. The maximum Canadian application rate is 5.55 kg a.i./ha.

The American and Canadian use patterns were compared. The Canadian formulation type of end-use products and use sites are among those registered in the United States. The maximum Canadian application rate is encompassed by the rates assessed in the RED and TRED. Based on this, it was concluded that the USEPA RED and TRED for maleic hydrazide are an adequate basis for the re-evaluation of uses of maleic hydrazide in Canada.

All current uses are being supported by the registrant(s) and were therefore considered in the re-evaluation of maleic hydrazide. Appendix II lists all maleic hydrazide products registered as of 11 March 2008 under the authority of the *Pest Control Products Act*.

## 3.0 Impact on Human Health and the Environment

In its 1994 RED, the USEPA concluded that the use of products containing maleic hydrazide registered at the time of the RED publication would not pose unreasonable risks or adverse effects to humans or the environment and are therefore eligible for reregistration. After the RED, the USEPA published a TRED in 2005 that includes an aggregate risk assessment that met the *Food Quality Protection Act* requirements.

### 3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

In Canada, exposure to maleic hydrazide may occur through consumption of food and water, through residential exposure, while working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

#### 3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

The USEPA's toxicological endpoints for assessing risk from occupational exposure are summarized in Appendix III.

Workers can be exposed to maleic hydrazide when mixing, loading or applying the pesticide and when entering a treated site to conduct activities such as scouting or handling of treated crops.

##### 3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

It was determined that there were several exposure scenarios for occupational handlers of maleic hydrazide. Specifically, exposure via the dermal and inhalation routes could occur during foliar application by groundboom, backpack sprayer or aircraft. In the RED, the USEPA determined

that there were no relevant endpoints of toxicological concern, and a quantitative exposure and risk assessment was not conducted. The USEPA required basic personal protective equipment during handling activities. In the 2005 TRED, however, an inhalation endpoint was selected for short- and intermediate-term exposure.

The PMRA generated the short- and intermediate-term MOEs in Table 1 below based on the USEPA's inhalation endpoint selected in its TRED, the maximum Canadian application rate and the screening level assumptions of area treated per day. Based on this, the Canadian uses of maleic hydrazide result in an acceptable occupational risk.

**Table 1 Occupational Margins of Exposure Using Canadian Pesticide Handlers Exposure Database Tables, PMRA Tier I Assumptions for Area Treated per Day and Canadian Maximum Application Rates**

| Scenario | Inhalation Unit Exposure (µg/kg a.i.) | Rate (kg a.i./ha) | Area Treated (ha) | MOEs[1] |
|---|---|---|---|---|
| Mixer/loader soluble granules, open mixing, **groundboom** on potato | 1.02 | 3.39 | 300 | 1933 |
| Applicator **groundboom**, open cab, on potato | 0.96 | 3.39 | 300 | 1318 |
| Mixer/loader/applicator, open mixing, **groundboom** on potato | 1.98 | 3.39 | 300 | 1007 |
| Mixer/loader soluble granules, **aerial** (potato) | 1.02 | 3.39 | 490 | 1198 |
| Mixer/loader/applicator **airblast** to trees | 6.82 | 5.55 | 16 | 33 333 |
| Mixer/loader/applicator **low-pressure handwand**, wettable powder, open mixing, on turf | 2261 | 4.8 | 2 | 94 |

[1] $\text{MOE} = \frac{\text{NOAEL}}{\text{Exposure}}$

Exposure = inhalation unit exposure (100% absorption assumed) × application rate × area treated per day

The PMRA requires baseline personal protective equipment (long-sleeved shirt, long pants, shoes and socks) during mixing, loading, application, cleanup and repair to further protect workers. In addition, the PMRA requires chemical-resistant gloves during mixing/loading and when applying by hand-held equipment. For basic hygiene purposes, and since the granules can break down into inhalable particles during shipping, handling, pouring and application, the PMRA also requires that handlers wear a dust mask during mixing/loading activities. The proposed label amendments are listed in Appendix IV.

#### 3.1.1.2 Postapplication Exposure and Risk

In the RED, the USEPA determined that there was a low potential for exposure of workers to maleic hydrazide during postapplication activities because applications were made at the early stages of plant development and because of its low volatility. Therefore, occupational postapplication risk to agricultural workers was not assessed quantitatively. A restricted-entry interval of 12 hours for all maleic hydrazide agricultural use products was required.

This was considered applicable to the Canadian situation, and the PMRA requires a 12-hour restricted-entry interval to further protect workers from postapplication exposure. Proposed label amendments are listed in Appendix IV.

### 3.1.2 Non-Occupational Exposure and Risk Assessment

#### 3.1.2.1 Residential Exposure

Residential exposure is estimated using the MOE approach described in Section 3.1.1. The toxicological endpoint selected by the USEPA for assessment of risk from residential exposure is described in Appendix III.

Homeowners can be exposed to maleic hydrazide when entering a treated site. Toddlers can be exposed via "hand-to-mouth" and "object-to-mouth" activities and through incidental soil ingestion.

In Canada and the United States, maleic hydrazide is registered for use on the edges of residential lawns, on golf course roughs and on ornamental trees and shrubs. Since maleic hydrazide is to be applied by professional applicators only, residential handler scenarios (i.e. scenarios involving individuals who mix, load and apply the pesticide product) were not assessed and only postapplication exposures are of potential concern for residential assessment. Also, minimal non-occupational postapplication exposure is expected from the use on golf course roughs, based on the timing and locations of use (golfers are not expected to spend significant amounts of time in golf course roughs); therefore, no assessment was conducted for this use.

The USEPA identified a potential for residential incidental oral exposure to children; therefore, risk to toddlers from postapplication exposure (incidental oral exposure) was assessed. Toddler "hand-to-mouth", "object-to-mouth" and "incidental soil ingestion" MOEs were estimated to be 254, 1000 and 76 000, respectively (target MOE of 100) based on a maximum application rate of 8.97 kg a.i./ha on turf.

The RED adequately addressed exposure scenarios associated with the residential uses of maleic hydrazide (i.e. on ornamentals) in Canada. Thus, the conclusions derived from the RED are considered applicable to the Canadian situation. No further mitigation measures are required.

### 3.1.2.2 Exposure From Food and Drinking Water

No acute endpoints of concern were identified by the USEPA, and maleic hydrazide was classified as a Group E carcinogen (no evidence of carcinogenicity). On this basis, no acute or cancer risk assessments were conducted.

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the RED, it is expressed as the chronic population adjusted dose (cPAD). The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation.

Maleic hydrazide is moderately persistent under anaerobic conditions. Based on this, and on the extreme mobility of maleic hydrazide, the USEPA determined that there was a potential for contamination of groundwater. There is also a potential for contamination of surface waters if maleic hydrazide is washed into anaerobic zones by rainfall events occurring soon after application (see Section 3.2.1 for further details on the environmental fate of maleic hydrazide).

Screening models were used to estimate drinking water concentrations (EDWCs) from use of maleic hydrazide on fallow land in the United States. These models assumed one application of maleic hydrazide at the maximum rate of 10.1 kg a.i./ha, using both aerial and ground application. Surface water peak and annual average EDWCs were calculated to be 500 and 3.46 ppb, respectively. The groundwater peak and annual average EDWCs were both estimated to be 0.011 ppb.

An unrefined Tier I chronic dietary risk assessment based on exposure from food and drinking water was conducted. The USEPA estimated exposure from food and drinking water (based on the average surface water concentration of 3.46 ppb) to represent 52% of the cPAD for the subpopulation of concern, children 1–2 years old, which represents acceptable risk. This analysis included conservative assumptions, including 100% crop treated, tolerance-level residues and default processing factors.

This assessment is considered to be relevant to Canada because it included all potential sources of exposure relevant to the Canadian use pattern, it used tolerances for onion and potato and it was based on application rates encompassing the maximum Canadian application rates. Therefore, the USEPA assessment is considered applicable to the Canadian situation and no additional mitigation measures are required.

### 3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to maleic hydrazide (i.e. from food, water and residential exposures).

Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures and are discussed in the previous section.

The short- and intermediate- term aggregate risk assessments are based on contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

The USEPA estimated short-term aggregate risk based on combined risks from average (chronic) food and drinking water exposure as well as short-term incidental oral exposure of children. This assessment is considered to be conservative based on tolerance level residues, screening level Tier I expected environmental concentrations (EECs), the maximum application rate of 10.1 kg a.i/ha, and the maximum percent cropped area (87%). Based on the resulting short-term aggregate MOE of 102 for the subpopulation of concern (children 1–2 years old), the USEPA concluded that aggregate exposure was not of concern.

Overall, the Canadian aggregate exposure scenarios were adequately addressed by the USEPA's aggregate risk assessment. Therefore, the USEPA's aggregate exposure conclusions are considered applicable to the uses of maleic hydrazide in Canada.

### 3.1.3 Cumulative Effects

The USEPA has not determined whether maleic hydrazide has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that maleic hydrazide does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

## 3.2 Environment

### 3.2.1 Environmental Risk Assessment

Maleic hydrazide was found to be non-persistent in soil under aerobic conditions, moderately persistent under anaerobic conditions and highly mobile in the environment. It was considered to have the potential to reach surface water via runoff and/or spray drift and to contaminate groundwater via leaching. The potential for bioaccumulation of maleic hydrazide was found to be very low ($\log K_{ow} < 0.6$).

To assess the ecological risk of maleic hydrazide to both terrestrial and aquatic non-target plants and animals, the USEPA calculated risk quotients (RQs) based on appropriate toxicity endpoints and expected environmental concentrations (EECs) and compared the resulting RQs to corresponding levels of concern (LOCs). The USEPA conclusions were as follows.

- Maleic hydrazide was found to be practically non-toxic to honey bees, and the potential for maleic hydrazide to have adverse effects on non-target insects is expected to be minimal.
- Based on an assessment of the risk to birds, a use pattern with application rates of ≤10.1 kg a.i./ha is not considered to present a potential risk to birds.

- The EECs estimated for mammals were below the LOCs; thus, minimal risk to non-endangered or endangered mammals is anticipated.
- Maleic hydrazide is practically non-toxic to honey bees, and the potential for maleic hydrazide to have adverse effects on non-target insects is expected to be minimal.
- Considering estimated maximum aquatic EECs based on runoff from ground application, and both runoff and drift from aerial and airblast applications, risks to non-endangered or endangered aquatic organisms are expected to be minimal because aquatic EECs were lower than the $LC_{50}$s for fish and invertebrates.
- Given aquatic EECs were below the level of concern, risks of concern to endangered or non-endangered aquatic plants are not expected.
- There is a risk of concern for semi-aquatic plants, from application rates as low as 2.2 kg a.i./ha, which indicates that almost all registered uses of maleic hydrazide are likely to pose a risk to semi-aquatic plants growing in off-site wet areas. There is also a high risk to terrestrial plants from the registered use in rights-of-way at application rates of 6.7 kg a.i./ha.

Based on risks of concern to terrestrial and semi-aquatic plants, the USEPA required an advisory statement on how to minimize runoff and a limitation of one application per year for use on fallow land, lawns, turf and rights-of-way to reduce ecological exposure.

The USEPA's assessment was based on maximum application rates, which encompass the Canadian maximum application rate. The American use pattern for maleic hydrazide encompasses the Canadian use pattern, and the USEPA's risk-reduction measures should be applied to Canadian products containing maleic hydrazide as follows:

- Recommendation of one application per year to rights-of-way
- Addition of an advisory label statement on all end-use products to mitigate runoff
- Requirement for terrestrial buffer zones for all end-use products of maleic hydrazide to protect terrestrial plants from spray drift

Proposed label amendments are listed in Appendix IV. Inputs to buffer zone models are described in Appendix V.

### 3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal Toxic Substances Management Policy, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

The federal Toxic Substances Management Policy (TSMP) and PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of maleic hydrazide. The PMRA has reached the following conclusions.

- Maleic hydrazide does not bioaccumulate. The *n*-octanol–water partition coefficient (log $K_{ow}$) is -0.99 at pH 7, which is below the TSMP Track 1 cut-off criterion of ≥5.0. Maleic hydrazide was not found to be persistent. The aerobic soil half-life is <24 hours, which is below the TSMP Track 1 criterion of 180 days. Maleic hydrazide does not meet all TSMP Track 1 criteria; thus, it is not a candidate for Track 1 classification.

- Hydrazine was identified by the PMRA as a potential microcontaminant based on the manufacturing process, and batch analysis data of the technical grade active ingredient showed that hydrazine is present at levels below 2.3 ppm in the technical product. This is below the level of concern of 15 ppm, as reported in the USEPA RED and TRED documents. The technical grade active ingredient is not expected to contain other impurities of human health or environmental concern as identified in DIR98-04, Section 2.13.4, or TSMP Track 1 substances as identified in DIR99-03, Appendix II.

- Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document,* published on 31 May 2006.

## 4.0 Proposed Re-evaluation Decision

The PMRA has determined that maleic hydrazide is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use products must be amended to include the label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrant of the technical grade active ingredient is required to submit data as a condition of continued registration under section 12 of the *Pest Control Products Act*. Appendix I lists data requirements.

## 5.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED and TRED documents for maleic hydrazide are available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

## List of Abbreviations

| | |
|---|---|
| λ | wavelength |
| ADI | acceptable daily intake |
| a.i. | active ingredient |
| ASAE | American Society of Agricultural Engineers |
| CAS | Chemical Abstracts Service |
| cPAD | chronic population adjusted dose |
| cRfD | chronic reference dose |
| DACO | data code |
| $EC_{25}$ | environmental concentration to 25% |
| EDWC | estimated drinking water concentration |
| EEC | expected environmental concentration |
| g | gram(s) |
| h | hour(s) |
| ha | hectare(s) |
| kg | kilogram(s) |
| km | kilometre(s) |
| $K_{ow}$ | *n*-octanol–water partition coefficient |
| $LC_{50}$ | lethal concentration to 50% |
| LOEL | lowest observed effect level |
| mg | milligram(s) |
| MOE | margin of exposure |
| MRL | maximum residue limit |
| nm | nanometre(s) |
| NOAEL | no observed adverse effect level |
| NOEC | no observed effect concentration |
| NOEL | no observed effect level |
| OECD | Organisation for Economic Co-operation and Development |
| Pa | Pascal(s) |
| pH | -log10 hydrogen ion concentration |
| PIC | Prior Informed Consent |
| p*K*a | -log10 acid dissociation constant |
| PMRA | Pest Management Regulatory Agency |
| ppb | parts per billion |
| ppm | parts per million |
| RED | Reregistration Eligibility Decision |
| RQ | risk quotient |
| $t_{1/2}$ | half-life |
| TRED | Tolerance Reassessment Eligibility Decision |
| TSMP | Toxic Substances Management Policy |
| USEPA | United States Environmental Protection Agency |
| UV | ultraviolet |

## Appendix I Additional Data Requirements

Based on preliminary calculations, the PMRA does not require aquatic buffer zones for maleic hydrazide. However, aquatic buffer zone calculations were based on limited toxicity data. Consequently, that decision is to be considered interim. As a condition of continued registration, the following data are required to confirm that aquatic buffer zones are not required to adequately protect sensitive habitats. The registrants of maleic hydrazide are required to provide these data within the timelime specified in the decision letter the PMRA will send.

- DACO 9.3.3 - *Daphnia* sp. - Chronic (Life-cycle)
- DACO 9.4.5 - Chronic (Mollusc or Crustacean)
- DACO 9.5.3.1 - Cold Water Fish (rainbow trout) - Early Life Cycle

These studies must be conducted with a Canadian end-use-product or a product with equivalent formulation and guarantee, and according to the appropriate USEPA Office of Prevention, Pesticides and Toxic Substances or Organisation for Economic Co-operation and Development guidelines.

# Appendix II Registered Products Containing Maleic Hydrazide as of 11 March 2008

| Registration Number | Marketing Class | Registrant | Product Name | Formulation Type | Guarantee (%) |
|---|---|---|---|---|---|
| 19153 | Technical | Chemtura Canada Co/Cie. | Technical Maleic Hydrazide | Dust | 97% min. |
| 26599 | Technical | Drexel Chemical Co. | Drexel Maleic Hydrazide 97% | Solid | 97% |
| 18143 | Commercial | Chemtura Canada Co/Cie. | Royal MH 60SG Plant Growth Regulator | Soluble granules | 60% |
| 27654 | Commercial | Drexel Chemical Co. | Drexel Sprout-Stop 60 SG | Soluble granules | 60% |

# Appendix III Toxicological Endpoints for Maleic Hydrazide Health Risk Assessments

| Exposure Scenario | Dose (mg/kg bw/day) | Study | UF/SF or MOE[a] |
|---|---|---|---|
| Chronic dietary (all populations)[b] | Dose for risk assessment (NOEL) = 25<br><br>cRfD = cPAD = 0.25 | Chronic toxicity/carcinogenicity study in the rat<br>(systemic LOEL = 500 mg/kg bw/day based on decreased body weight) | 100 |
| Incidental oral Short-term (1–30 days) and intermediate-term (1–6 months)[b] | Systemic toxicity NOEL = 29 | "Co-critical" 52-week feeding study in the dog<br>(systemic LOEL = 87 mg/kg bw/day based on decreased weight gain in both sexes and reduced heart weight in males) | 100 |
| Cancer (oral, dermal, inhalation)[b] | Classification: "Group E"—evidence of non-carcinogenicity to humans. | | |

[a] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments. MOE refers to desired margin of exposure for occupational or residential assessments.

[b] From USEPA TRED (2005).

# Appendix IV Label Amendments for Products Containing Maleic Hydrazide

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

I) The following statements must be included in the **PRECAUTIONS** section.

Wear a long-sleeved shirt, long pants, shoes and socks during mixing, loading, application, cleanup and repair for all methods of application. In addition, wear chemical-resistant gloves during mixing/loading and when applying by hand-held equipment.

Wear a dust mask during mixing/loading activities.

II) The following statements must be included in the **DIRECTIONS FOR USE** section.

DO NOT enter or allow worker entry into treated areas for 12 hours following application.

Field sprayer application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground.

Airblast application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. DO NOT apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

Aerial application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. DO NOT apply when wind speed is greater than 16 km/h at flying height at the site of application. DO NOT apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length MUST NOT exceed 65% of the wing- or rotorspan.

**Buffer Zones:**

Use of the following spray methods or equipment DO NOT require a buffer zone: hand-held or backpack sprayer and spot treatment.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelterbelts, woodlots, hedgerows, riparian areas and shrublands).

| Method of Application | Crop | | Buffer Zones (metres) Required for the Protection of: |
|---|---|---|---|
| | | | Terrestrial Habitat |
| Field sprayer | Potato, onion (sprout inhibition)<br><br>Tree/shrub, non-crop grass (growth control) | | 1 |
| Airblast | Tree/shrub (early season) | | 10 |
| Aerial | Onion | Fixed or rotary wing | 15 |
| | Potato | Fixed or rotary wing | 20 |

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture.

II) The following statements must be included in the **ENVIRONMENTAL HAZARDS** section.

TOXIC to non-target terrestrial plants. Observe buffer zones specified under **DIRECTIONS FOR USE**.

Do not contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to, heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g. soils that are compacted or fine textured such as clay).

Avoid application of this product when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

# Appendix V Inputs to Buffer Zone Models

| Ground Use Data (from Canadian labels) | | | | |
|---|---|---|---|---|
| **Crop** | **Formulation Type** | **Method of Application** | **Number of Applications** | **Maximum Application Rate (g a.i./ha)** |
| Potato sprout inhibition | Wettable granules | Field (medium) | 1 | 3390 |
| Onion sprout inhibition | Wettable granules | Field (medium) | 1 | 2250 |
| Tree/shrub growth control (airblast) | Wettable granules | Early airblast | 1 | 5550 |
| Tree/shrub growth control (boom) | Wettable granules | Early airblast | 1 | 5550 |
| Non-crop grass growth control | Wettable granules | Field (medium) | 1 | 4800 |

| Model Input Data for Aquatic Buffer Zones (from 1994 RED) | | |
|---|---|---|
| | | **Value used in calculation** |
| Half-life for aquatic buffer zones | Stable | |
| Choice of toxicity endpoint for amphibian buffer zones | Rainbow trout | 1/10 $LC_{50}$ = 143.5 mg a.i./L |
| Most sensitive freshwater species | *Lemna gibba* | NOEC = 38.6 mg a.i./L |
| Choice of toxicity endpoint for marine buffer zones | *Lemna gibba* | NOEC = 38.6 mg a.i./L |

| Model Input Data for Terrestrial Buffer Zones (from 1994 RED) | | |
|---|---|---|
| Half-life for terrestrial buffer zones | Soil B | $t_{1/2}$ = 27 days |
| Most sensitive terrestrial plant species $EC_{25}$ for vegetative vigour | Onion | 590 g/ha |

| Aerial Use Data (from Canadian labels) | | | | |
|---|---|---|---|---|
| **Crop** | **Formulation Type** | **Registration Number** | **Number of Applications** | **Maximum Application Rate (g a.i./ha)** |
| Potato | Wettable granule | 18143 | 1 | 3390 |
| Potato | Wettable granule | 27654 | 1 | 3390 |
| Onion | Wettable granule | 18143 | 1 | 2250 |
| Onion | Wettable granule | 27654 | 1 | 2250 |

| Product Information for Aerial Use | | |
|---|---|---|
| **Parameter** | **Value** | |
| | **Registration Number 18143** | **Registration Number 27654** |
| Aircraft type | Fixed-wing and rotary aircraft equipment | Fixed-wing and rotary aircraft equipment |
| ASAE spray quality | Medium | Medium |
| Carrier | Water | Water |
| Product guarantee (g a.i./L) | 600 | 600 |
| Specific gravity of end-use product (g/L) | 1000 | 1000 |
| Minimum spray volume (L/ha) | 100 | 100 |
| Water content of product (%) | 0 | 0 |
| Wind speed (km/h) | 16 | 16 |
| Temperature (°C) | 25 | 25 |
| Relative humidity (%) | 50 | 50 |

# References

## List of Studies/Information Submitted by Registrant (Unpublished)

| PMRA Document Number | Reference |
|---|---|
| 1576956 | Technical Chemistry file MAH-CZG-1. Technical Data Sheet, Active Ingredient Specifications, Control Test AC-1013 Maleic Hydrazide in MH Tech and AC-1061 % MH in Royal MH-30, Collaborative Study of Maleic Hydrazide Residue Analysis., DACO: 2.1,2.10,2.11.1 |
| 1577788 | 1989, Technical Chemistry file MAH-DRX-2. Drexel Maleic Hydrazine -95% Physical and Chemical Characteristics, DACO: 2.14 |
| 1577782 | 1989, Technical Chemistry file MAH-DRX-2. Drexel Maleic Hydrazine -95% Technical Grade Product Identity and Composition, DACO: 2.11 |
| 1577025 | Technical Chemistry file MAH-DRX-2. Confidential Attachments - Manufacturing Summary, Description of Starting Materials, Detailed Description of Production Process, Discussion of Formation of Impurities, Analytical Methods, Analytical Methods for Certificate |
| 1576948 | 1989, Technical Chemistry file MAH-CZG-1. Compositional Analysis for Maleic Hydrazide, DACO: 2.13.3 |

## Additional Information Considered (Published)

The European Commission's *Directive 2003/31/EC* (EC 2003)
http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:101:0003:0009:EN:PDF